sequence itself has not changed. This is evident from looking at the version number given in the current record, "Z70522.*1*". Had the sequence changed at all in any of the updated records, it would have been given a version number of one greater than the prior version of the sequence (e.g. "Z70522.*2*" would be the version number the first time the sequence changes, etc.). If the Examiner is still in doubt, a comparison can be made of the sequences set forth in the current entry for Z70522 and the original 1997 entry, copies of which are provided here as Exhibit A. For future reference, prior versions of GenBank records can be accessed in the "Sequence Revision History" section of the NCBI website (at (world wide web) ncbi.nlm.nih.gov/entrez/sutils/girevhist.cgi). In summary, no new matter has been added to the specification, and the objection should be withdrawn.

Written description rejection

The Examiner rejected claims 1, 7, 9-12, 15, and 19-23 on the basis that they fail to comply with the written description requirement of 35 USC § 112. However, the Examiner again fails to provide an explanation as to why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. Thus, the Examiner has not met the initial burden of providing a proper rejection under the written description requirement of 35 USC § 112, (see Fed. Reg., Vol. 66, No. 4, January 5, 2001, p. 1105); therefore, the rejection should be withdrawn.

With regards to the abstracts submitted as Exhibits B-D with Applicants previous response, the Examiner stated that "the articles may actually disclose the sequences of the portions of the subject promoter." This indeed was the purpose of submitting the abstracts, i.e. to demonstrate that given a promoter-containing nucleotide sequence, one skilled in the art knows that sub-fragments of the sequence that retain promoter activity can be readily identified. Thus, given Applicants' disclosure of a promoter-containing nucleotide fragment, and the description provided in the specification that a promoter includes segments of the specifically disclosed sequences that retain promoter function (p. 7, lines 6-9), one skilled in the art would appreciate that the specification describes the claimed subject matter.

For the above reasons, it is believed that the written description rejection under 35 U.S.C. § 112, 1st paragraph should be withdrawn.

Enablement rejection

The Examiner rejected claims 1, 7, 9-12, 15, and 19-23 on the basis that they fail to comply with the enablement requirement of 35 USC § 112.

In the middle paragraph on page 5 of the office action, the Examiner stated that "Applicants argue the examiner has not provided any reasons why guidance must be provided to enable the claims (response, paragraph bridging pages 5-6)". However, this is a misquote. What Applicants said in their previous response was that "the examiner has not provided any reasoning as to why ***such*** guidance must be provided..." (emphasis added). This argument was in response to the Examiner's assertion that the specification does not provide any guidance as to the sequences within the promoter of bases 156-1708 of SEQ ID NO:42 that are ***essential*** to tissue specific activity. However, applicants are not specifically claiming "the minimal promoter fragment of SEQ ID NO:42 essential for fruit-associated expression". Thus, a showing of the "essential" regions responsible for the claimed promoter activity is not necessary.

The Examiner states that "in the absence of guidance, one skilled in the art would be left to make ***fragments of any and all sizes*** from the 1735 bp sequence of SEQ ID NO:42, which amounts to undue experiments." (Emphasis added). This is an exaggeration. Given the size of this sequence (1735 bp) and having been provided the location of the TATA box (see Figure 3), one would have to make just a few 5' deletions to approximate the length of the sequence necessary for fruit-specific expression. For example, Adam et al. (attached as Exhibit B) constructed six deletion derivatives of a 3319 nucleotide promoter sequence to ascertain a 383 bp region of the promoter, between nucleotides –1472 to –1089, responsible for tissue-specific activity (see Figure 3A and Table 1). Golden et al. (attached as Exhibit C) constructed 9 deletion fragments of an 8kb 5' UTR region of the endothelin-1 gene to determine regions necessary for basal regulation, thrombin-stimulated induction, and full expression of a reporter gene (see Figure 4 and discussion on p. L860). As the starting sequences used by Adam et al. and Golden et al. were significantly larger than Applicants' 1735 bp sequence (i.e. 3319 bp and 8kb, respectively), it is reasonable to assume that one skilled in the art would not have to make very many fragments in order to further characterize the region of the claimed promoter responsible for fruit-associated expression. This amounts to routine, not undue, experimentation.

In the paragraph at the top of page 6 of the office action, the Examiner suggests that claim 1 is not enabled because it is not predictive which sub-fragments of the disclosed sequence would retain fruit-associated promoter activity, and that further experimentation would be required. However, the issue is not whether further experimentation would be required, but rather whether such experimentation would be undue. For the reasons already presented above, it is clear that undue experimentation would not be required to identify such sub-fragments.

In the middle paragraph on page 6 of the office action, the Examiner suggests that Applicants submit a declaration showing how fragments of the disclosed sequence having fruit-associated functional activity have been identified. While further identification of the precise sequence responsible for the fruit-associated promoter activity may be of interest to an academic investigator, the assignee of the claimed invention is a business, and having already identified a suitable promoter for fruit-associated expression, has no desire to use employee time and resources to carry out experimentation that has no business value. However, one desiring a promoter for fruit-associated expression would most certainly carry out such routine experimentation in order to avoid licensing a patent that is limited to the subject matter of Applicants' claim 5.

For the above reasons, the claimed invention is supported by an enabling disclosure, and the rejection under 35 U.S.C. § 112, 1st paragraph should be withdrawn.

Closing remarks

It is believed that all of the rejections are overcome, and that the claims are in condition for allowance. The examiner is encouraged to telephone the undersigned to discuss any further issues that may need resolution prior to allowance.

Respectfully submitted,

Dated: November 3, 2003

Jan P. Brunelle Reg. No. 35,081

EXELIXIS, INC.
170 Harbor Way
P.O. Box 511
South San Francisco, California 94083-0511
Telephone: (650) 837-8180
Facsimile: (650) 837-8234